# Modern Concepts of Cardiovascular Disease

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## THE PATHOGENESIS OF SYSTEMIC ARTERIAL EMBOLISM IN RHEUMATIC HEART DISEASE*

Precisely how clots form in the left auricle in rheumatic heart disease is not known; how they are mobilized is also a matter of conjecture. The mechanism of thrombosis in a cardiac cavity is essentially that of any blood vessel, and must be explained in accordance with the three postulates of de Senac[1] and Virchow:[2] endothelial damage, coagulability of the blood, and sufficient retardation of blood flow. It is a reasonable premise that the source of the thromboplastin initiating a thrombus is situated nearby.[3] In cavitary thrombosis of the heart, this source presumably is damaged endothelium in an adjacent position. Studies of the auricular wall underlying 192 auricular clots have shown "very typical and substantial wall lesions" in about half the cases.

As judged by gross diagnosis, the right auricular clots were predominantly of nonrheumatic origin and the left auricular clots predominantly of rheumatic origin (Table I). In 108 of these cases, the diagnosis was established microscopically: of 82 clots arising from lesions of "coronary" type, 79 were in the right auricle; of 26 clots of rheumatic origin, 25 were in the left auricle.

Table I

*Distribution of 192 Auricular Thrombi in Nonrheumatic Heart Disease and Rheumatic Heart Disease*†

| | Nonrheumatic heart disease | % | Rheumatic heart disease | % |
|---|---|---|---|---|
| Right | 86 | 65 | 10 | 16 |
| Right and Left | 27 | 20 | 17 | 29 |
| Left | 19 | 15 | 33 | 55 |
| Total | 132 | | 60 | |

†From Söderström.[4]

Although lesions underlying thrombi in the left auricular appendage were surprisingly scarce in Söderström's studies,[4] the frequency of cellular infiltration in the auricular appendages of patients with rheumatic mitral stenosis attests to latent wall damage in a high proportion of patients with rheumatic heart disease. Stasis in these chambers with wall damage encourages thrombosis. The inherent thrombotic tendency of any type of wall damage apparently determines the degree of stasis required to initiate cardiac mural thrombosis. If the tendency is strong, thrombosis may occur even though the blood flow is only mildly retarded and the time for interaction, therefore, somewhat brief.

Myocardial infarction is a highly thrombotic lesion. It is limited largely to the left ventricle and the right auricle, and "coronary" mural thrombi are concentrated in these two cavities. Although stasis increases the danger of thrombosis in these cavities (for example, in congestive heart failure), thrombi can form readily even without stasis.[5]

The inherent thrombotic tendency of a rheumatic lesion is mild.[6] Thrombosis occurs only when stasis is greatly protracted. Although the left auricle and its appendage are involved in nearly all instances of acute rheumatic carditis,[7,8] thrombosis seldom occurs until there has been a long period of stasis induced by obstruction at the mitral valve, with dilatation and reduced contractility of the auricle.

### Thrombi in Rheumatic Heart Disease

Nearly all left auricular thrombi in rheumatic heart disease occur predominantly with mitral stenosis. The highest frequency, 84 per cent as observed at cardiotomy, is found in pure mitral stenosis with auricular fibrillation, as compared with only 3 per cent in pure mitral stenosis with normal sinus rhythm.[9]

In auricular fibrillation, there is no demonstrable increase in the incidence of endothelial dam-

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age in the left auricle. The two types of tissue change associated with rheumatic infection, *i.e.*, (*a*) the Aschoff body, and (*b*) a type of chronic inflammation considered characteristic by Pappenheimer, Von Glahn,[10] and others, are not more frequent in auricular fibrillation. On the contrary, the Aschoff bodies are actually scarcer in fibrillation than in normal rhythm, and scarcer still in patients with thrombi.[11,12,13] The chronic inflammatory changes, however, have been found in the wall of the left auricle in a high proportion of patients with chronic rheumatic heart disease, irrespective of rhythm.[14] They conceivably could be the foci of thrombosis, if the other two thrombotic factors were effective. As to coagulability of the blood, there is no evidence of increase save that which might be due to the generally greater age of the patients.

The third factor, reduction of blood flow from the left auricle to the left ventricle, deserves consideration as to degree and duration. Stenosis of the mitral valve converts a normally variable, pulsatile flow into an even flow, increases pressure within the auricle, and usually causes dilatation. Dilatation of the auricle, since it is associated with an increased residual volume, represents stasis. The degree of dilatation is highly variable: it may be slight, moderate, or marked, and is determined by the degree of pressure and the elasticity of the auricular wall.[15]

Lewis found no greater left auricular enlargement in auricular fibrillation than in normal rhythm in the fluoroscopic examination of 30 patients with pure mitral stenosis. Wood,[16] however, observed a significant difference at cardiotomy. One hundred fifty cases of mitral stenosis with normal rhythm had an average enlargement of 1.45, and with auricular fibrillation, 1.78. Soloff, Zatuchni, Stauffer and Kelly,[17] measuring the volume of the left auricle by angiocardiographic techniques, found the normal volume to be 100 ml. From their observations, the volume in pure stenosis with normal rhythm was 425 ml.; in auricular fibrillation, 543 ml. There was thus a fourfold to fivefold increase in volume in both normal rhythm and auricular fibrillation, and a slightly greater residual volume in auricular fibrillation. This reflection of the slightly greater degree of stasis in auricular fibrillation would not seem to be as important a thrombotic factor as the greater duration of the stasis, since the patients with auricular fibrillation had an average age of 44, and those with normal rhythm, 34.

In mitral stenosis, auricular fibrillation identifies longstanding rheumatic heart disease, that is, an older lesion with more prolonged stasis, but it does not in itself greatly exaggerate the degree of stasis over that found in normal rhythm. Because the patient is older, coagulability of the blood may be greater, and the endothelium has been subjected to the damaging effect of the prolonged stasis. All three thrombotic factors are simultaneously at a maximum. Auricular fibrillation, therefore, frequently coincides with left auricular thrombosis but does not primarily cause it. The two conditions, apparently, result from coincident causes.

All the foregoing applies only to patients with predominant mitral stenosis. In mitral regurgitation, the occurrence of fibrillation denotes a longer duration of an opposite state, *i.e.*, a varying flow of blood through the auricle.

### Mobilization of Thrombi

The fact that approximately half of all left auricular thrombi are ejected and the other half retained has not been adequately explained, even theoretically. Certain mechanical forces are probably of primary importance in mobilizing thrombi, although humoral factors, probably fibrinolytic, theoretically may disintegrate or lessen the firm consistency of the clot.[18] The forces that tend to expel thrombi are essentially the same that normally tend to prevent their formation, *i.e.*, an active blood flow, contraction of the auricular wall, and a possible distortion of the auricular wall coinciding with ventricular systole and diastole.[19-22]

There is no evidence as to whether normal rhythm or established auricular fibrillation is more likely to mobilize thrombi. Although systemic arterial embolism occurs four times as frequently in fibrillation as in normal rhythm, the incidence is entirely in proportion to the frequency of left auricular thrombi in each state.

The change from auricular fibrillation to normal rhythm is occasionally followed by embolism. Conversely, embolism not uncommonly coincides with, or soon follows, either a paroxysm of auricular fibrillation or the establishment of this arrhythmia. Among 150 cases of conversion from auricular fibrillation to normal rhythm studied by Sokolow and Ball,[23] only two had emboli at the time of conversion, but in seven they appeared at the time of a subsequent relapse from normal rhythm to auricular fibrillation. Embolism occurred during paroxysms of auricular fibrillation in five out of 13 patients with rheumatic heart disease studied by the author.[24] In the case of seven patients observed by Daley and associates,[25] "the onset of fibrillation was probably concurrent with the embolic incident." Harris and Levine,[26] and Raynaud and associates,[27] found that in many instances embolism occurred soon after the arrhythmia was established. The occasional causative relationship of these changes of rhythm with embolism is accepted by most clinicians, although the explanation is uncertain.

What is the difference in contraction of the left auricle with normal rhythm and auricular fibrilla-

tion? Left auricular pressures in mitral stenosis with normal rhythm, and with auricular fibrillation determined by catheterization, have shown an increase in pressure in mid and late diastole in normal rhythm. This supposedly is synchronous with left auricular contraction, and is indicated by the presence of giant "a" waves, which are absent in auricular fibrillation.[28] How much actual contraction of the distended auricle is reflected by this rise in pressure is speculative. Hecht and Lange[29] state that the auricular contraction in normal sinus rhythm in mitral stenosis contributes surprisingly little to the flow. At cardiotomy for mitral stenosis, both the body and the appendage of the auricle are inert to ordinary vision. Without inspecting the ventricle, the rhythm of the distended auricle cannot be accurately stated. By angiocardiography, Soloff and associates[17] failed to observe any appreciable variation in the size of the left auricle during the cardiac cycle in patients with mitral stenosis, whether the rhythm was normal or auricular fibrillation. Arterial embolism can be correlated with either a change from auricular fibrillation to normal rhythm or the reverse. Therefore, the long-accepted theory that embolism, which occurs with a change from auricular fibrillation to normal rhythm, is caused by a return of contraction of the auricle is open to doubt.

With these observations, any alteration of auricular contraction would not seem as significant as the abrupt change in the pattern of ventricular contraction. We can only speculate as to whether sudden alteration in ventricular rhythm brings about mobilization of auricular thrombi. Conceivably, it might do so by some change in the distorting effect of ventricular systole and diastole on the auricle, or by some other means. A sudden change in ventricular rhythm, as well as a change in auricular contraction, may explain dislodgment of an auricular thrombus. Final explanation must await further evidence.

No correlation has been established between the dislodgment of cavitary thrombi in general and the onset of a rapid heartbeat, whether it is sinus tachycardia, auricular flutter,[30] or paroxysmal supraventricular tachycardia. Although exercise increases the rate of mitral valve flow in mitral stenosis, there is no convincing evidence that effort increases embolism in rheumatic heart disease. On the contrary, Sprague and Westinghouse[31] found that of 77 presumed embolic arterial occlusions in 38 patients with rheumatic heart disease and auricular fibrillation, over 90 per cent occurred during ordinary daytime activity or when the patients were at rest. Activity preceding or accompanying embolism, they concluded, was only coincidental.

No crucial study has been made of the relation of digitalis to the mobilization of left auricular thrombi. The only definite clinical correlation with embolism is the occasional change from normal rhythm to fibrillation, or the reverse. The precipitating causes of embolism which occurs without a change of rhythm remain indefinite and unexplained.

## Summary

Auricular clots presumably are distributed according to the location of endocardial damage: in nonrheumatic heart disease, in the right auricle; in rheumatic heart disease, in the left auricle.

Left auricular thrombosis in rheumatic heart disease appears to be a result mainly of prolonged left auricular stasis. The primary correlate, auricular fibrillation, is related only statistically, not causally, to the high incidence of thrombosis. It is a hallmark of prolonged stasis when found in mitral stenosis, but only slightly increases the degree of auricular stasis. There is no adequate explanation for the mobilization of left auricular thrombi in the majority of instances. The occurrence of embolism cannot be correlated with anything save occasionally a change in the rhythm of ventricular contraction from regular to irregular, or vice versa. Mobilization of left auricular thrombi in rheumatic heart disease, therefore, must be regarded in the main as a fortuitous event.

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